2551-1001
PATENT

IN THE U.S. PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of	Appeal No.
Roberto VILLA et al.	Conf. 4029
Application No. 10/009,532	Group 1615
Filed December 12, 2001	Examiner Humera Sheikh

CONTROLLED RELEASE AND TASTE MASKING ORAL PHARMACEUTICAL COMPOSITIONS

APPEAL BRIEF

MAY IT PLEASE YOUR HONORS:

(i) **Real Party in Interest**

The real party in interest in this appeal is the assignee, Cosmo Technologies Limited of Wicklow, Ireland.

(ii) **Related Appeals and Interferences**

None.

(iii) **Status of Claims**

Claims 25-39 are pending in this application. The present appeal is taken from the final rejection of all the pending claims.

(iv) **Status of Amendments**

An Amendment After Final Rejection canceling claims 1-24 and adding new claims 25-39 was filed on August 9, 2006. An Advisory Action was mailed on August 30, 2006 in response to the

Amendment After Final Rejection. The Advisory Action indicated that the new claims would be entered for purposes of appeal.

(v) **Summary of Claimed Subject Matter**

Claim 25 (the sole independent claim on appeal) recites a controlled release composition comprising one or more active ingredients that are incorporated into a particular matrix-based structure. The composition includes a hydrophilic phase, an amphiphillic phase, and a lipophillic phase.

These three phases are formed as two distinct matrices (page 4, line 20 to page 6, line 15; and the examples).[1]

Importantly, claim 25 requires that the claimed second matrix, which includes the lipophilic phase and the amphiphilic phase, is dispersed throughout the hydrophilic first matrix (page 4, lines 25-30; and page 5, lines 1-5).

The claimed composition also includes at least one active ingredient present in at least the lipophilic and amphiphilic phases (page 8, line 34 to page 10, line 14).

Appellants have discovered that this structure controls not only the release of the active from the composition but also the influx or penetration of water and/or biological fluids towards the center of the composition, which in turn serves to regulate the dissolution rate of an active ingredient in aqueous

or biological fluids(page 10, lines 15-30). For example, the claimed composition can be used to control the release kinetics of active ingredients in the gastrointestinal tract and to mask unpleasant tastes by controlling the dissolution rate of bad-tasting ingredients.

(vi) **Grounds of Rejection to be Reviewed on Appeal**

The sole issue on appeal is whether claims 25-39 would have been obvious, within the meaning of 35 USC §103(a), in view of AKIYAMA (EP 0514008 A1) taken alone.

(vii) **Argument**

AKIYAMA discloses at page 7, lines 40-45 gastrointestinal mucosa-adherent compositions in one of three forms:

A) a composition in which a viscogenic agent is dispersed at least in the neighborhood of a surface layer of a matrix particle containing an active ingredient and a polyglycerol fatty acid ester,

B) a composition in which a viscogenic agent has been dispersed in the neighborhood of the surface layer of a matrix particle containing the active ingredient and a lipid, and

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[1] As is evident from the specification for example at pages 5-6, the term "matrix" is used broadly in the present application to denote a carrier substance.

C) a composition in which a matrix particle has been coated with a coating composition comprising or containing a viscogenic agent (page 7, lines 40-45).

AKIYAMA further states that a lipid can be incorporated into the matrix particles of compositions A and C (page 7, lines 46-54).

In relating the disclosure of AKIYAMA to the claims on appeal, the viscogenic agent of the reference could be considered to be a hydrophilic phase, the polyglycerol fatty acid ester an amphiphilic phase, and the lipid a lipohilic phase.

Thus, what is conspicuously absent from AKIYAMA is any disclosure or suggestion of a lipophilic phase and an amphiphilic phase in the form of a second matrix dispersed throughout a hydrophilic first matrix. To the contrary, the viscogenic agent of AKIYAMA, which corresponds to the hydrophilic phase of the claims on appeal, is in all cases dispersed or coated onto the outer surface of a particle that may contain the lipophilic and amphiphilic substances. In other words, AKIAYAMA disclose coating a particle or core with a viscogenic agent to form a "reservoir" type composition.

That structure bears no similarity to the claimed multi-matrix system, in that the lipophilic and amphiphilic phases of the reference are not part of a second matrix that is dispersed at all, much less throughout a first hydrophilic matrix.

The layer of viscogenic agent on the surface of the particle or core allows the AKIYAMA composition to adhere to the digestive tract and remain there for a prolonged period of time to increase the bioavailability of an active ingredient dispersed in the composition (abstract and pg. 1, lines 9-34).

The claimed structure utilizes a different mechanism of release. The dissolution rate of an active ingredient is controlled by regulating the influx or penetration of water and/or biological fluids towards the center of the composition with matrix configuration as recited in the claims.

In view of the above, it is believed to be apparent that the disclosure of AKIYAMA stands in contrast to the claimed invention.

Indeed, the Examiner acknowledges that AKIYAMA does not disclose or suggest the claimed positional interrelationship between the recited ingredients. Rather, the Advisory Action mailed on August 30, 2006 merely contends that "[w]hile there may be slight structural differences between the AKIYAMA formulation and the instant invention, the results attained by AKIAYAMA are similar to that claimed, such as the controlled release composition".

The position of the Examiner is further explained in the Official Action mailed on January 11, 2006, which states that

> The prior art initially teaches and is directed to a composition that comprises identical components (lipophilic, amphiphilic, hydrophilic substances), used for

> the same field of endeavor as desired by Applicants. Therefore, it is the position of the Examiner, that given the teachings of AKIYAMA et al. to formulate controlled release pharmaceutical compositions for the delivery of drugs using a variety of components, such as viscogenic agents, lipids, etc. in a matrix system used in the gastrointestinal tract, the instant invention, when taken as a whole would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. (Official Action mailed January 11, 2006, page 7).

The rejection on appeal thus entirely disregards the manner in which the components are dispersed throughout the claimed composition. As a result, the rejection on appeal plainly fails to provide the requisite factual basis to support a sustainable *prima facie* case of obviousness.

As AKIYAMA disclose a distinct gastrointestinal mucosa-adherent composition, a divergent mechanism of release and the Official Action fails to make a *prima facie* case of obviousness, it is believed that the rejection should not be affirmed.

It is accordingly believed that the rejection of claims 25-39 for obviousness based on AKIYAMA alone is improper and should be reversed. Such action is respectfully requested.

Respectfully submitted,

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(viii) **Claims Appendix**

25. A controlled release composition, comprising:

a hydrophilic first matrix comprising a lipophilic phase and an amphiphilic phase,

wherein said lipophilic phase and said amphiphilic phase are in a second matrix together, and said second matrix is dispersed throughout the hydrophilic first matrix,

wherein said lipophilic phase comprises lipophilic compounds and an active ingredient at least partially incorporated in said lipophilic phase, and

wherein said amphiphilic phase comprises an active ingredient at least partially incorporated in said amphiphilic phase.

26. The controlled release composition according to claim 25, wherein the lipophilic phase consists of lipophilic compounds with a melting point below 90°C.

27. The composition according to claim 25, further comprising compounds that are polar lipids of type I or II, ceramides, glycol alkyl ethers, esters of fatty acids with polyethylene glycols or diethylene glycols.

28. The composition according to claim 25, wherein the lipophilic phase comprises one or more compounds selected from the group consisting of unsaturated or hydrogenated alcohols or fatty acids, salts, esters or amides thereof, mono-, di- or triglycerides of fatty acids, the polyethoxylated derivatives thereof, waxes, and cholesterol derivatives.

29. The composition according to claim 25, wherein the hydrophilic matrix consists of hydrogel-forming compounds.

30. The composition according to claim 29, wherein the hydrophilic matrix consists of compounds selected from the group consisting of acrylic or methacrylic acid polymers or copolymers, alkylvinyl polymers, hydroxyalkylcellulose, carboxyalkyl-cellulose, polysaccharides, dextrins, pectins, starches and derivatives, alginic acid, natural or synthetic gums, and polyalcohols.

31. The composition according to claim 25, further comprising a gastro-resistant coating.

32. The composition according to claim 31, wherein the gastro-resistant coating consists of methacrylic acid polymers or cellulose derivatives.

33. The composition according to claim 25, wherein said composition is in the form of tablets, capsules or minitablets.

34. The composition according to claim 26, wherein said composition is in the form of tablets, capsules or minitablets.

35. The composition according to claim 25, in which the active ingredient belongs to the therapeutical classes of analgesics, antitussives, bronchodilators, antipsychotics, selective β 2 antagonists, calcium antagonists, antiparkinson drugs, non-steroidal anti-inflammatory drugs, antihistamines, antidiarrheals and intestinal antiinflammatories, spasmolytics, anxiolytics, oral antidiabetics, cathartics, antiepileptics, topical antimicrobials.

36. The composition according to claim 25, wherein the active ingredient is selected from the group consisting of mesalazine (5-aminosalicylic acid), budesonide, metformin, octylonium bromide, gabapentin, carbidopa, nimesulide, propionylilcarnitine, isosorbide mono- and dinitrate, naproxen, ibuprofen, ketoprofen, diclofenac, thiaprophenic acid, nimesulide, chlorhexidine, benzydamine, tibezonium iodide, cetylpyridinium chloride, benzalkonium chloride, and sodium fluoride.

37. The composition according to claim 25, further comprising bioadhesive substances.

38. A pharmaceutical composition, comprising the composition according to claim 25, in the form of tablets chewable or erodible in the buccal cavity or in the first portion of the gastrointestinal tract.

39. The method according to claim 25, wherein the amphiphilic matrix comprises 5 to 95% by weight of an active ingredient.

(ix) **Evidence Appendix**

None.

(x) **Related Proceedings Appendix**

None.